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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PRIEBE, SCOTT DAVID	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 12/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/391,861	THOMASON ET AL.	
	Examiner	Art Unit	
	Scott D. Priebe, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-13,39 and 41-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-13,39 and 41-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *attached* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 11/7/05 has been entered.

The Group and/or Art Unit designation of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Primary Examiner Scott D. Priebe, Ph.D., Group Art Unit 1633.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Claims 5, 7, 13, 42, and 43 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may not depend from another multiple dependent claim and must depend from the multiple claims in the alternative only. Claim 5 depends from multiple dependent claim 2, and depends from claim 2 and either claim 1 or claim 39. Claims 13 and 42 depend from claim 9, which is a multiple dependent claim through its dependence from multiple dependent claim 8, and they depend from claim 9 and either claim 1 or claim 39.

Applicant is advised that should claim 5 be found allowable, claims 13 and 42 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The only difference between these claims is that claim 13 recites that the polypeptide can be isolated from the culture, and claim 42 does not. However, claim 43 further limits claim 42 by the added step of isolating the polypeptide, and there is no situation in which a polypeptide expressed in one culture can be isolated, but expressed in a different cell culture cannot be isolated at least to some degree of purity. Consequently, the additional limitation of claim 13 is inherent or implicit in the process of claim 42.

Claim Rejections - 35 USC § 101 & 112

Claims 1-6, 7-13, 39, and 41-43 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. In the absence of a specific and substantial asserted utility, credibility of such use cannot be addressed. The grounds of rejection set forth below is basically the same as presented in previous office actions. Some points have been expanded upon, with some additional supporting evidence provided, and some redundant discussion has been omitted.

The instant application has provided a description of an isolated nucleic acid molecule encoding a so-called "FGF-like polypeptide" protein and the protein encoded thereby. The

specification teaches that the "FGF-like" polypeptide is structurally similar to known members of the fibroblast growth factor (FGF) family, with the highest sequence identity being 32% identity to FGF-6 and 28% identity to FGF-4 for the murine FGF-like protein SEQ ID NO: 4 (spec., page 19), and appears to contain a signal peptide indicating that it is a secreted protein. Northern hybridization of the nucleic acid encoding the murine (SEQ ID NO: 3) and human (SEQ ID NO: 1) FGF-like protein against a panel of mRNA isolated from various mouse or human tissues, respectively, revealed strong expression only in adult liver in both mouse and human, and weak expression in human adult lung and fetal liver (spec., pages 80-81). The specification notes that this near exclusivity of expression makes it unique among known FGF family members. Finally, the specification (page 4) describes 6-8 week-old transgenic mice comprising an ectopic gene that encodes the murine FGF-like polypeptide under control of an unspecified promoter. The specification mentions making transgenic mice where the coding sequence for the FGF-like polypeptide is placed under control of an apolipoproteins E promoter (liver specific) or a β-actin promoter (ubiquitous), but does not indicate which of these was actually used in making the transgenic mice described. The mice displayed reduced body weight, reduced liver and spleen weight and increased thymus weight as a percentage of total body weight, and in females, poorly developed ovaries without significant follicular development.

Based upon the homology of the FGF-like polypeptide to members of the FGF family, its likely secretion into the bloodstream, and its expression in the liver, the specification (page 5) speculates that the protein "may" exert is effects on distal sites, and "may" provide benefits in the stimulation of cells within or near the liver, regulation of intestinal cell activity, stimulation of pancreatic beta islet cells, regulation of neuronal cells, stimulation or inhibition of

angiogenesis, stimulation of epithelium or mesenchymal components of granulation tissue, stimulation of corneal epithelium, lens, or retinal tissue, regeneration of renal tubules, hematopoietic cell regulation, regulation of hair follicle growth, or regulation of pulmonary epithelium, particularly as a therapeutic pharmaceutical composition. The specification does not describe how the FGF-like protein might "stimulate" or "regulate" these tissues, what it would stimulate them to do or what process it would regulate or in which way, or what the consequence of exposure to exogenous FGF-like protein would be. With respect to stimulating liver cells, this purported function is at odds with the results obtained with the transgenic mice that ectopically over-express the FGF-like polypeptide, since they had an underdeveloped or underweight liver. Thus it is left to one of skill in the art to determine which of these possible activities, if any, the FGF-like polypeptide may exert and the nature or outcome of such activities or use as a therapeutic composition. The specification merely invites one of skill in the art to determine if the FGF-like polypeptide stimulates any of these tissues and in what way, and to determine if the FGF-like polypeptide regulates a process in these tissues, what process, and in which way it regulates it.

The specification (pages 5-6) also speculates that the FGF-polypeptide or the nucleic acid encoding it "may" be useful as an inhibitor of growth or fat deposition or "may" be useful in the treatment of diagnosis of a medical condition such as cirrhosis or other toxic insult of the liver; inflammatory bowel disease, mucositis, Crohn's disease, or other gastrointestinal abnormality; diabetes; neurodegenerative diseases; wounds; damage to the corneal epithelium, lens, or retinal tissue, damage to renal tubules as a result of acute tubular necrosis; hematopoietic cell reconstitution following chemotherapy; multiple sclerosis; alopecia; diseases or abnormalities of

androgen target organs; infantile respiratory distress syndrome, bronchopulmonary dysplasia, acute respiratory distress syndrome, or other lung abnormalities; or tumors of the eye or other tissues. The specification (page 6) then contradictorily suggests that antibodies or other inhibitors of the binding of the FGF-like protein to its unknown receptor may be used to treat these same diseases. It is not reasonable that both the polypeptide and an inhibitor of the polypeptide or its expression would both be useful for treating the same medical condition. The specification does not explain how the FGF-like polypeptide, its coding nucleic acid, antibodies or inhibitors might be used to diagnose any of these conditions or diseases, i.e. it does not disclose whether an increased or decreased expression would be diagnostic or in which tissues or cells such diagnostic expression would occur. It is left to one of skill in the art to determine which, if any, of these diseases can be diagnosed or treated with any of the compounds relating to the FGF-like polypeptide described in the specification, and to devise how such diagnosis or treatment should be carried out.

Nucleic acid encoding the murine FGF-like polypeptide was used to make the transgenic mouse described above. The specification des not assert any use for the mice specifically, and appears to rely on them solely to identify a phenotype resulting from the ectopic overexpression of the polypeptide. There is no assertion that the mice could be used as a model for a disease process, for example. The specification leaves it to one of skill in the art to devise a practical use, if any, for these mice.

The specification does not identify nor describe determining any specific biochemical or physiological function of the FGF-like polypeptide at the level of cells, tissues or whole organism. No assay for the function of the FGF-like polypeptide is disclosed. The specification

mentions the FGF-polypeptide, the nucleic acid encoding it, antibodies against the FGF-like polypeptide, agonists and antagonists of the polypeptide, and antisense oligonucleotides directed against the gene encoding the FGF-like polypeptide. The specification does not disclose any assay or determination of the biological function of the FGF-like protein, an agonist of the protein, an antagonist of the protein, or an inhibitor of its expression. In other words, the consequences of administering any of the contemplated compounds to a cell, tissue, or organism were unknown at the time the instant application was filed, both to the inventors and to those of skill in this art. In essence, the specification merely provides an invitation to those of skill in the art to determine biochemical and physiological functions of these products, and devise assays for those functions.

The assertions of the vague and undefined potential utilities present in the specification appear to be based upon functions or activities that have been suggested for other members of the FGF family. It was recognized in the art that FGFs are members of a protein family which has demonstrated a broad range of biological activities involving cell proliferation and differentiation during embryogenesis and post-natally and tissue maintenance, but that individual members of the FGF family have distinct functions and activities, i.e. one member of the FGF family cannot, in general, substitute for another member. While there is some overlap in function or activity between individual members, their range of function precludes *a priori* determination of the function of a newly discovered member of the family, such as the FGF-like polypeptides of SEQ ID NOs: 2 and 4. Galzie et al. (Biochem. Cell Biol. 75: 669-685, 1997), discloses that the FGF family is complex and diverse (see abstract). Table 1 of Galzie et al. details the biological significance of the first 9 members of this protein family, wherein none of the associated

functions are found in common with any other family member. The family is named after the initial discovery of FGF1 and FGF2, which are mitogenic for fibroblasts. However, some FGF members are not mitogenic for fibroblasts. For example, FGF-7 is secreted by fibroblasts, but is mitogenic for epithelial cells (page 671, col. 2). Goldfarb (Cytokine & Growth Factor Rev. 7(4): 311-325, 1996) teaches that the members of the FGF family mediate diverse response during embryogenic, fetal and postnatal development in complex interactions between other FGF members and other non-FGF regulatory molecules. The various FGF members bind to one or more of seven different FGF receptors (FGFR), and the expression of the FGF members and the receptors is strictly regulated both spatially and temporally during development. Different FGFs and FGFRs are involved in different processes during development, in some cases cooperatively and sometimes antagonistically. The effect of exposing a given cell type to a specific FGF depends on the cell type and what FGFRs it is expressing at the time of exposure. In an experiment similar to that described in the instant specification, Hu et al. (Mol. Cell. Biol. 18(10): 6063-6074, Oct. 1998) describe transgenic mice that ectopically overexpress FGF-18 under control of a liver specific promoter. The native FGF-18 gene was found to be expresses primarily in lung and kidney, and little or not at all in liver. The resulting mice had increased liver and small intestine mass as a fraction of body weight, and FGF-18 was found to induce proliferation of a variety of specific cells of epithelial and mesenchymal origin. These results show that the tissue that predominately expresses an FGF member may not be the tissue that responds to the FGF. In contrast to these results, ectopic expression of the instant FGF-like polypeptide in transgenic mice resulted liver hypotrophy, not hypertrophy, as one would expect if the polypeptide promoted proliferation of liver cells, as suggested in the specification.

The instant situation is directly analogous to that addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sup. Ct, 1966) and *In re Kirk*, 153 USPQ 48 (CCPA 1967). These cases involved the utility of specific members of a structurally related class of compounds (steroids) or methods of making such specific members, where other structural homologs had known physiological activities and practical uses that varied between the specific compounds of the class. The applications failed to disclose any specific activity or use for the claimed compounds or the compounds that could be made with the inventions. The courts held that the inventions did not meet the utility requirement, regardless of whether it could be shown later that the compound in question did have a practical use. As in these cases, the instant specification relies on the structural homology between the FGF-like polypeptide encoded by the claimed nucleic acid and other members of the FGF family, some of which had known diverse activities and uses, and the suggestion that the FGF-like polypeptide of the invention might have an activity or use shared with another member of the FGF family, but without any experimental evidence to show that the FGF-like polypeptide in fact possessed any activity or use in common with any of the other FGF members, or if so, what that activity or use was or might be.

The instant specification provides no more than suggestions for various avenues of experimental investigation to determine what biological or pharmacological activities the FGF-like polypeptide might have and what practical use the nucleic acids, polypeptides, antibodies, etc. may be derived from such activities. A "patent is not a hunting license. It is not the reward for the search, but compensation for its successful conclusion," *Brenner* at 696 and *Kirk* at 53.

Claims 1-6, 7-13, 39, and 41-43 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial

asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's arguments filed 11/7/05 have been fully considered but they are not persuasive. The credibility of the claimed invention is not at issue since the specification does not assert a specific and substantial utility for the claimed invention. It is acknowledged that the FGF-like polypeptide of the invention is likely to have a credible, specific and substantial practical use. The issue here however is that the application does not disclose what that use is. Rather, the specification is no more than an invitation to one of skill in the art to go and find out for themselves what that use is. Applicant alleges that the specification page 5, lines 23-25, page 6, lines 4-5) contains the assertion that the nucleic acids and polypeptides encoded thereby "are useful for treating and preventing liver related disease s and disorders" (page 9 of the reply). In response, the original specification makes no such assertion. The specification states that the "FGF-like polypeptides and nucleic acid molecules of the invention may be used for therapeutic or diagnostic purposes to treat, prevent and/or detect a medical condition such as cirrhosis or other toxic insult of the liver ..." along with a laundry list of other medical conditions that the polypeptides "may" be used for therapeutic or diagnostic purposes to treat, prevent and/or detect. The specification further states (page 6, lines 12-14) the "invention also provides for the use of antibodies or other inhibitors of the binding of FGF-like polypeptide to its receptor for the treatment of the same diseases listed above." The specification does not teach that the polypeptide or nucleic acid may be used specifically to treat liver disease and one would not reasonably suppose that both the polypeptide and an inhibitor of the polypeptide could both be used to treat liver disease. Furthermore, the specification provides no evidence that would

provide a basis for one of skill in the art to believe that the polypeptide could be used to treat a liver disease. The only experimental evidence in the specification relating the polypeptide to the liver is that in transgenic mice that overexpress the polypeptide, the liver is underdeveloped. As described in Galzie and in Goldfarb, different members of the FGF family play a variety of different roles in embryonic or fetal development, but that this role is complex and depends on the coordinated expression of the individual FGF and other FGFs and growth factors. The phenotype observed in the transgenic mouse does not provide evidence that the FGF-like polypeptide normally plays a role in liver development, only that its ectopic overexpression disrupts normal liver development. Whether the observed effect is due to over-stimulation or over-inhibition of a process normally mediated by the FGF-like protein or whether the effect is due to an abnormal interference by inappropriately expressed FGF-like protein is a question that can only be answered by future experimentation, and not by consultation of the specification, which does not even speculate on why or how the ectopic expression of the FGF-like polypeptide led to the observed phenotype. Furthermore, this evidence does not suggest that supplying an excess of the FGF-like polypeptide to the liver of a postnatal animal would have any effect similar to that observed in the transgenic mice, where the FGF-like polypeptide affected development either directly or indirectly. As shown in Hu, one cannot predict on the basis of where the FGF is expressed, what the target cells would be.

The rejection of the claims set forth in the Office action of 10/6/04 (pages 16-20) for failing to provide an adequate written description or enablement (for how to make) of the claims as directed to generic embodiments is hereby withdrawn. The claims require that species differing from the nucleotide sequence SEQ ID NO: 1 or 3 or a nucleotide sequence that encodes

SEQ ID NO: 2 or 4 have the physical relationship of hybridizing to the nucleotide sequence SEQ ID NO: 1 or 3 or a nucleotide sequence that encodes SEQ ID NO: 2 or 4 under the recited high stringency conditions. Such variant nucleotide sequences could have been readily envisioned by one of skill in the nucleic acid art using SEQ ID NO: 1-4. The issue is whether one would have known what to do with such variant sequences when the structural differences lead to a variant polypeptide having lost the function of SEQ ID NO: 2 or 4 due to the variations, or how to make structurally different variants that retained the function of SEQ ID NO: 2 or 4. These issues relate to whether the specification and claims meet the utility and enablement requirements, rather than the written description requirement. Had the claims also required a particular function, then the written description or how-to-make enablement requirement would be at issue. Since the application as filed fails to meet the utility requirement, the issue of enablement for how to use the variants of SEQ ID NO: 1 or 3 embraced by the claims is moot.

Claims 1-5, 7-13, and 41-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The hybridization conditions recited in claim 1(d), parts (3) and (4) are new matter. Applicant points to page 10, lines 3-13 as support for these conditions. However, a careful reading of page 10, lines 9-13, reveals that the conditions recited separately in parts (d)(3) and (d)(4) are all part of a single set of hybridization conditions. This rejection would be overcome

by combining parts (d)(3) and (d)(4) as a single set of conditions, i.e. by deleting "; or (4)" from lines 15-17 and inserting "or" before "(3)" in line 12.

Claims 7 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites the limitation ""the native FGF-like gene" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Similarly, there is no nexus between the recitation of "FGF-like polypeptide" in claim 12 and the subject matter of claims 1 and 2, from which claim 12 depends. It is unclear what the "FGF-like polypeptide" has to do with the nucleic acid molecule or nucleotide sequence of claim 2.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002

do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 2, 4, 8, 9, 11, and 39 are rejected under 35 U.S.C. 102(a) as being anticipated by GenBank Acc. No. AQ175436, 10/17/98, as evidenced by Kennel, D.E. (Progr. Nucl. Acid Res. Mol. Biol. 11: 259-301, 1971) with respect to claim 1 and dependents.

GenBank Acc. No. AQ175436 discloses a nucleic acid molecule, wherein nucleotides 128-483 are over 93% identical to nucleotides 1-356 of instant SEQ ID NO: 1. Nucleotides 128-303 are identical to nucleotides 1-176 of SEQ ID NO: 1 and nucleotides 128-378 differ form nucleotides 1-251 by only three single nucleotide mismatches, and so would clearly hybridize to SEQ ID NO: 1 under the most stringent conditions. See Kennell (para. bridging pages 260-261), which teaches that duplexes of 25-50 paired, contiguous nucleotides, depending on G+C content, are as stable as much longer duplexes, i.e. 25-50 paired, contiguous nucleotides are all that are required for maximum stability of the duplex. As per claim 39, this prior art sequence comprises at least 16 nucleotides of SEQ ID NO: 1, and it also encodes the first 29 amino acids of SEQ ID NO: 2. The document also discloses a plasmid vector containing the nucleic acid molecule and a prokaryotic host cell containing the vector.

Claims 1 and 39 are rejected under 35 U.S.C. 102(a) as being anticipated by GenBank Acc. No. AV050323, 6/22/99, as evidenced by Kennel, D.E. (Progr. Nucl. Acid Res. Mol. Biol. 11: 259-301, 1971) with respect to claim 1 and dependents.

Claims 2, 4, 8, 9, and 11 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over GenBank Acc. No. AV050323, 6/22/99, as evidenced by Kennel, D.E. (Progr. Nucl. Acid Res. Mol. Biol. 11: 259-301, 1971) with respect to claims dependent from claim 1, and GenBank Acc. No. AQ175436.

GenBank Acc. No. AV050323 discloses a nucleic acid molecule that comprises a sequence (nucleotides 1-604) that is over 93% identical to nucleotides 437-640 of instant SEQ ID NO: 3. The nucleic acid comprises regions of 29, 55 (36/55 G+C), and 59 (36/59 G+C) nucleotides that are identical to regions of instant SEQ ID NO: 3. As a result, this nucleic acid would be expected to hybridize to instant SEQ ID NO: 3 under the most stringent hybridization conditions. See Kennell (para. bridging pages 260-261), which teaches that duplexes of 25-50 paired, contiguous nucleotides, depending on G+C content, are as stable as much longer duplexes, i.e. 25-50 paired, contiguous nucleotides are all that are required for maximum stability of the duplex.

With respect to claims 2, 4, 8, 9, and 11, GenBank Acc. No. AV050323 does not provide any details on clone 1810013H18. However, the standard method for preparing such clones in the art is to insert the cDNA into a bacterial plasmid that is then used to transform a suitable strain of *E. coli*. For example, see GenBank Acc. No. AQ175436.

Claims 1-5, 7-11, 13, 39, and 41-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Edwards et al., US 6,639,063, in claiming priority to 60/147,499, filed 8/5/99.

Edwards discloses a nucleic acid molecule, SEQ ID NO: 1353, that encodes a polypeptide, SEQ ID NO: 5213, that comprises the first 79 amino acids of instant SEQ ID NO: 2. Nucleotides 28-477 of SEQ ID NO: 5213 differ from nucleotides 1-451 of instant SEQ ID NO: 1 by only two mismatched nucleotides, which are separated by only two paired nucleotides (nucleotides 177-180 of SEQ ID NO: 1) and an indel mismatch (nucleotide 394 of SEQ ID NO: 1). Consequently, this prior art sequence would clearly hybridize to instant SEQ ID NO: 1 under the most stringent conditions. Edwards also discloses bacterial and eukaryotic expression vectors comprising this sequence under control of a promoter, host cells comprising the vector, and methods of producing the protein encoded thereby from the host cells in culture, which may then be purified from the culture media. The vector may be for production of the polypeptide encoded by the nucleic acid sequence alone, or a fusion polypeptide comprising the signal peptide of the polypeptide fused to a protein of interest.

See entire document, for example at col. 9, lines 1-19; col. 9, line 66 to col. 10, line 18; col. 12, lines 42-50; col. 14, lines 37-47; col. 15, lines 4-13; col. 16, line57, to col. 17, line 2; col. 17, lines 37-52; col. 19, lines 16-28; col. 21, lines 20-30; col. 22, lines 16-28 and 51-58; cols. 52-55, Example 20; cols. 88-91, Examples 46 and 47; Table I, col. 125, line 18; Table IVb, col. 389, line 37; and Table V, col. 492, line 15.

Conclusion

The art made of record and not relied upon is considered pertinent to applicant's disclosure. Applicant's attention is directed to US 6,716,626, the claims of which are directed to nucleic acid encoding human FGF-21. SEQ ID NO: 4 of this application discloses a polypeptide that differs from instant SEQ ID NO: 2 by a single amino acid at position 174, Leu vs. Pro, respectively. SEQ ID NO: 3 of this application differs from nucleotides 134-776 of instant SEQ ID NO: 1 by a single nucleotide (nt. 662 of instant SEQ ID NO: 1). Applicant is reminded that there is no potential interference unless the instantly claimed subject matter is patentable to Applicant. US 2001/0012628 describes a nucleotide sequence, SEQ ID NO: 1, that encodes a polypeptide, SEQ ID NO: 2, that is identical to instant SEQ ID NO: 2. This document has been made of record in application 09/644,052, which is a CIP of the instant application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe, Ph.D. whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe, Ph.D.
Primary Examiner
Art Unit 1633